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The overall goal of this research project was to investigate the mechanisms of long-term synaptic potentiation (LTP) at mossy fiber synapses in hippocampus, with particular emphasis on the modulation of LTP by amine neurotransmitters. During the first year of this grant, several studies were completed in which a number of hypotheses were tested for the mechanisms of LTP. We found that LTP of the mossy fiber synapses is due to an increase in the excitatory synaptic conductance with little or no change in the excitatory synaptic reversal potential, the inhibitory synaptic conductance, or the membrane properties of the postsynaptic neuron. During the first and second years of the grant, we explored the neuromodulation of LTP by norepinephrine (NE). We found that NE enhances the magnitude, duration, and probability of induction of LTP at mossy fiber synapses. We also tested a number of hypotheses for the mechanisms of the NE modulation of LTP. These included that the action of NE was due to disinhibition, increases in cyclic AMP, and β-adrenoceptors. During the second and third years of this grant, we explored the membrane actions of NE that could mediate the enhancement of LTP. For these studies, we used a newly developed preparation of acutely exposed hippocampal neurons and patch clamp techniques. We found that NE, through β-adrenoceptors and cyclic AMP, increased the activity of single calcium channels. During the third year of this grant, we explored the neuromodulation of LTP by muscarinic cholinergic receptors. We found that muscarine depresses LTP at mossy fiber synapses. We also have developed a new preparation of isolated mossy fiber synaptic terminals and have begun to explore the properties of single calcium channels in this preparation. Over the course of the entire project period, we have steadily progressed in our development of single cell computer models for simulating the behavior of hippocampal neurons.

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AMINE NEUROTRANSMITTER REGULATION OF LONG-TERM SYNAPTIC PLASTICITY IN HIPPOCAMPUS

AFOSR 85-0178

Final Technical Report

1 Summary

The overall goal of this research project was to investigate the mechanisms of long-term synaptic potentiation (LTP) at mossy fiber synapses in hippocampus, with particular emphasis on the modulation of LTP by amine neurotransmitters. During the first year of this grant, several studies were completed in which a number of hypotheses were tested for the mechanisms of LTP. We found that LTP of the mossy fiber synapses is due to an increase in the excitatory synaptic conductance with little or no change in the excitatory synaptic reversal potential, the inhibitory synaptic conductance, or the membrane properties of the postsynaptic neuron. During the first and second years of the grant, we explored the neuromodulation of LTP by norepinephrine (NE). We found that NE enhances the magnitude, duration, and probability of induction of LTP at mossy fiber synapses. We also tested a number of hypotheses for the mechanisms of the NE modulation of LTP. These included that the action of NE was due to disinhibition, increases in cyclic AMP, and β-adrenoceptors. During the second and third years of this grant, we explored the membrane actions of NE that could mediate the enhancement of LTP. For these studies, we used a newly developed preparation of acutely exposed hippocampal neurons and patch clamp techniques. We found that NE, through β-adrenoceptors and cyclic AMP, increased the activity of single calcium channels. During the third year of this grant, we explored the neuromodulation of LTP by muscarinic cholinergic receptors. We found that muscarine depresses LTP at mossy fiber synapses. We also developed a new preparation of isolated mossy fiber synaptic terminals and began to explore the properties of single calcium channels in this preparation. Over the course of the entire project period, we steadily progressed in our development of single cell computer models for simulating the behavior of hippocampal neurons.

2 Research Objectives

The research objectives for the funding period 1 April 1985–31 March 1988 were broadly as follows:

a) Test hypotheses for mechanisms of LTP at the mossy fiber synapse.

b) Test hypotheses associated with the noradrenergic modulation of LTP.

c) Investigate the neuromodulation of LTP by muscarinic cholinergic receptors.

d) Investigate the multiple types of calcium channels in hippocampal neurons.

e) Test the hypothesis that NE modulates voltage dependent calcium conductances.

f) Develop a preparation of isolated mossy fiber synaptic terminals for electrophysiological analysis.

g) Develop single neuron computer models.

For the most part, these objectives were the same as those outlined in the original grant application. The investigation of the neuromodulation of LTP by muscarinic cholinergic receptors, however, was not originally proposed, and the development of the isolated mossy fiber terminal preparation and single cell computer models were additional objectives that were added in Year 2 as part of supplemental funding.

3 Status of Research

3.1 Biophysical mechanisms associated with LTP at mossy fiber synapses

In previous work in collaboration with Dr. Thomas Brown, we investigated the biophysical properties of mossy fiber synaptic transmission using single-electrode voltage clamp methods. From the results of these studies, we formulated four hypotheses for the mechanisms of LTP at these synapses, which were tested and the studies completed during the first year of funding.

a) The first hypothesis was that LTP at these synapses could be due to a decrease in the feedforward or recurrent GABA-mediated inhibition. We had found that stimulating the mossy fibers results in an overlap in time of the excitatory and inhibitory inputs to CA3 pyramidal neurons. A long-term decrease in the inhibitory input could thus result in an apparent increase in excitatory input and represent a potential mechanism for LTP.

b) The second hypothesis was that LTP could be due to a long-term change in the excitability of the postsynaptic neuron. It had been suggested in previous work that LTP at mossy fiber synapses was heterosynaptic in that LTP induced in one mossy fiber input would result in LTP of a nonstimulated input. A change in the excitability or properties of the postsynaptic neuron could be one potential mechanism to explain such heterosynaptic LTP. In recent work, however, Higashima and Yamamoto (8) re-evaluated the previous findings and found that LTP at the mossy fiber input was probably not heterosynaptic but homosynaptic in a similar way to the Schaffer collateral or perforant path inputs.

c) The third hypothesis was that LTP of the excitatory input could be due to a change in the synaptic equilibrium potential resulting from changes in the selective permeability of the transmitter-gated ion channels or from the addition of ion channels with different selectivities.

d) The fourth hypothesis was that LTP was due to a change in the conductance of the excitatory synaptic input.

The testing of these four hypotheses was published in two reports (1, 7) and can be summarized as follows:

a) We found no evidence for a long-term depression of the inhibitory input that could explain LTP. If anything, there was a small increase in the inhibitory synaptic conductance.

b) We found no evidence for a change in excitability of the postsynaptic neuron. We found no change in spike threshold, membrane time constant, or input resistance (measured with a current step or current in the form of an alpha function).

c) We found no evidence for a change in the synaptic equilibrium potential during LTP. The reversal potential of mossy fiber excitatory postsynaptic potentials (EPSPs) was not significantly different before and during LTP.

d) We found that LTP was associated with an increase of approximately 50% in the excitatory synaptic conductance.

3.2 Modulation of LTP by norepinephrine

In 1984, we published a short report suggesting that NE through β-adrenoceptors could enhance the amplitude, duration, and probability of induction of LTP at mossy fiber synapses (9). A major emphasis during the period of 4/1/85–8/1/87 was to test a number of hypotheses resulting from that study. These included that the modulation of LTP is mediated through changes in feedforward or recurrent inhibition, that cAMP was involved in the modulation of LTP, and that the modulation of LTP by NE took place on the postsynaptic neuron. We also explored a number of related questions associated with each of these hypotheses as well as performed additional experiments that put the original findings on a firmer basis. The results of these studies have been published (10).

a) It had been suggested by Madison and Nicoll (12) that NE decreases the activity of interneurons, resulting in overall disinhibition of a slice. In principle, such a mechanism could explain the NE enhancement of LTP because it is well known that disinhibition, through blockade of GABAergic inhibition, results in greater LTP (16). We tested this hypothesis by first blocking GABAergic inhibition with 10 μM picrotoxin (PTX) and then testing whether isoproterenol could still enhance LTP. We found that the β-adrenoceptor agonist isoproterenol increased both the magnitude and probability of induction of LTP in the presence of PTX (10). The results suggest that NE is not enhancing LTP through a modulation of GABAergic inhibition, at least not $GABA_A$-receptor mediated inhibition.

b) It is well known that activation of β-adrenoceptors in the brain stimulates the synthesis of cAMP. A reasonable hypothesis for the action of NE on LTP is therefore that the effects of NE are mediated through increases in cAMP. We tested this hypothesis by using forskolin, a diterpene compound that rapidly and reversibly activates adenylate cyclase in a variety of preparations (14). The results supported the hypothesis that cAMP mediates the effects of NE. Forskolin at concentrations of 10–50 μM produced a significant increase in the magnitude and probability of induction of LTP (10).

c) Distinguishing between possible pre- or postsynaptic actions of NE in the enhancement of LTP was an extremely difficult task. We approached the problem by using the results of our previous experiments in which we found that propranolol, when added to normal saline, greatly diminished the probability of induction of LTP and that cAMP mimicked the effects of NE on LTP. Experiments were designed as follows: intracellular recordings were made under three different experimental conditions. Three groups of cells were used for the analysis, and all three groups were from slices bathed in propranolol. One group of cells was injected with 5'AMP, the inactive metabolite of cAMP, while the other two groups were injected with 8-bromo-cAMP, a phosphodiesterase-resistant analog of cAMP. The excitatory synaptic conductance was determined in the three groups of cells using voltage-clamp techniques. The 5'AMP group and one of the 8-bromo-cAMP groups were given tetanic stimulation to induce

LTP. The other 8-bromo-cAMP group was not given tetanic stimulation. We found that only the group of cells injected with 8-bromo-cAMP and receiving tetanic stimulation to the mossy fibers displayed significant LTP (10). In other words, the group of cells injected with 8-bromo-cAMP overcame the block of LTP by propranolol. 8-bromo-cAMP alone did not produce LTP in the absence of tetanic stimulation. These results support the hypothesis that at least part of the NE modulation of LTP takes place postsynaptically.

We also found that the group of cells injected with 8-bromo-cAMP had a significantly greater and longer lasting depolarization of the membrane potential during tetanic stimulation compared to the 5'AMP group. This suggests the hypothesis that the mechanism of enhancement of LTP by NE is through an increased depolarization during the tetanic stimulation. One explanation for this greater depolarization is that NE enhances voltage-dependent Ca currents.

3.3 Muscarinic receptor modulation of LTP

During the last year of funding, we began investigating the possibility that activation of muscarinic receptors in the CA3 subfield has effects on mossy fiber synaptic transmission in general, and on LTP in particular. The results were submitted for publication and have recently been accepted with revision by *Science*.

All of our experiments were done with the slices bathed in 10 μM PTX to block feedforward and recurrent inhibition. We found that muscarine, at a concentration of 1 μM, had no significant effect on mossy fiber evoked synaptic transmission measured under either current or voltage clamp conditions and stimulated at 0.2 Hz. In contrast, however, 1 μM muscarine significantly decreased the magnitude and probability of induction of LTP when present during the high frequency stimulus train (Figs. 1, 2, & 3). Muscarine (1 μM), when added *after* the high frequency train, had no effect on LTP. At higher concentrations (10 μM), muscarine also depressed the mossy fiber evoked response in the absence of high frequency stimulation. We feel that these results are extremely interesting, especially in light of the prominent role that ACh is reported to play in learning and memory. Muscarine has been shown to decrease calcium currents in CA3 neurons (2). Our working hypothesis is that the depression of LTP by muscarine is due to a decrease in calcium influx during the high frequency stimulus train. It is interesting that LTP at this synapse appears to be oppositely regulated by NE and muscarine.

3.4 Exposed neuron preparation, multiple types of calcium channels, and modulation of calcium conductance by NE

We made substantial progress in this area during the period of funding. The acutely exposed neuron preparation for biophysical studies is now routine in our lab, and modifications thereof (11) in other labs. The first complete description of this preparation was published in 1985 (6).

During the last two years of funding, we focused our efforts on the investigation of voltage-dependent Ca currents in acutely exposed granule cells. We investigated the effects of NE and related substances on these Ca currents. I will briefly summarize these results, but a more complete description is given in Gray and Johnston (4).

We initially used whole-cell recording techniques and perfused the inside and the outside of the cell with solutions formulated to block voltage-dependent sodium and potassium currents. The resulting whole-cell Ca currents appeared to consist predominantly of a high threshold type, except that the currents did partially inactivate during the command. We found that NE, isoproterenol, 8-bromo-cAMP, and forskolin enhanced the amplitude of the Ca currents. Clonidine, an α-adrenoceptor agonist, did not increase the Ca currents, but our experiments did not allow us to determine whether clonidine decreased the Ca currents.

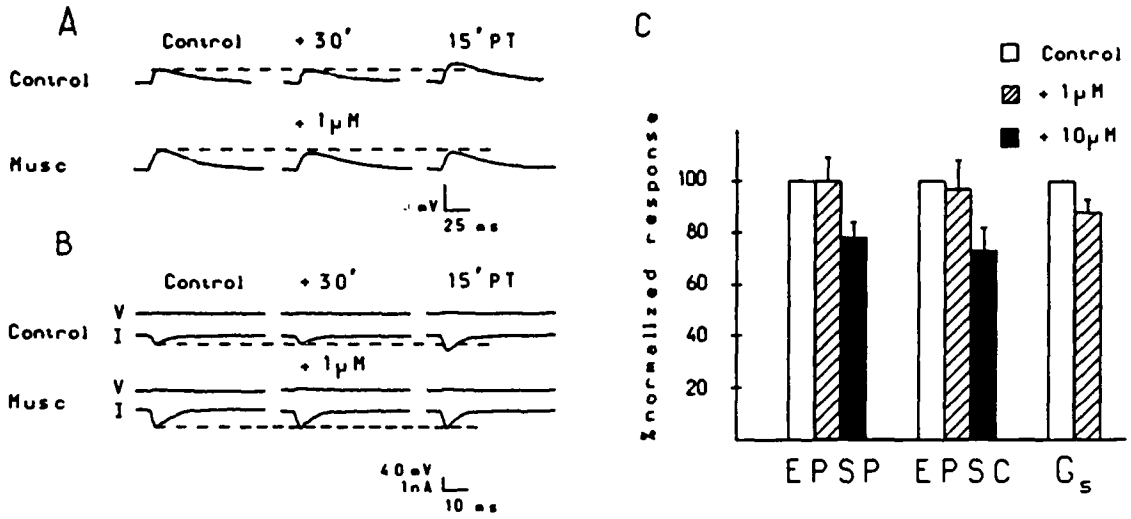

Fig. 1 The effects of muscarine on synaptic transmission and LTP. (A) Upper traces show that in a control cell the EPSP is stable for 30 min, but that 15 min after tetanus (15′ PT) an increase in amplitude is seen. The lower traces (Musc, different cell) reveal that 1 μM muscarine produced a small pretetanic depression of the EPSP, and prevented the development of LTP (15′ PT). (B) In a similar experiment under voltage clamp (V, membrane potential; I, clamp current), LTP in the control cell was seen as an increase in the EPSC, but in the muscarine treated cell no increase was apparent. (C) Summary of the actions of muscarine (1 and 10 μM) on synaptic transmission in the absence of tetanus. All data were normalized to control. (g_s, synaptic conductance, see text and Fig. 3.) EPSP: 1 μM, n=10; 10 μM, n=6: EPSC 1 μM, n=8; 10 μM, n=5: g_s 1 μM, n=5.

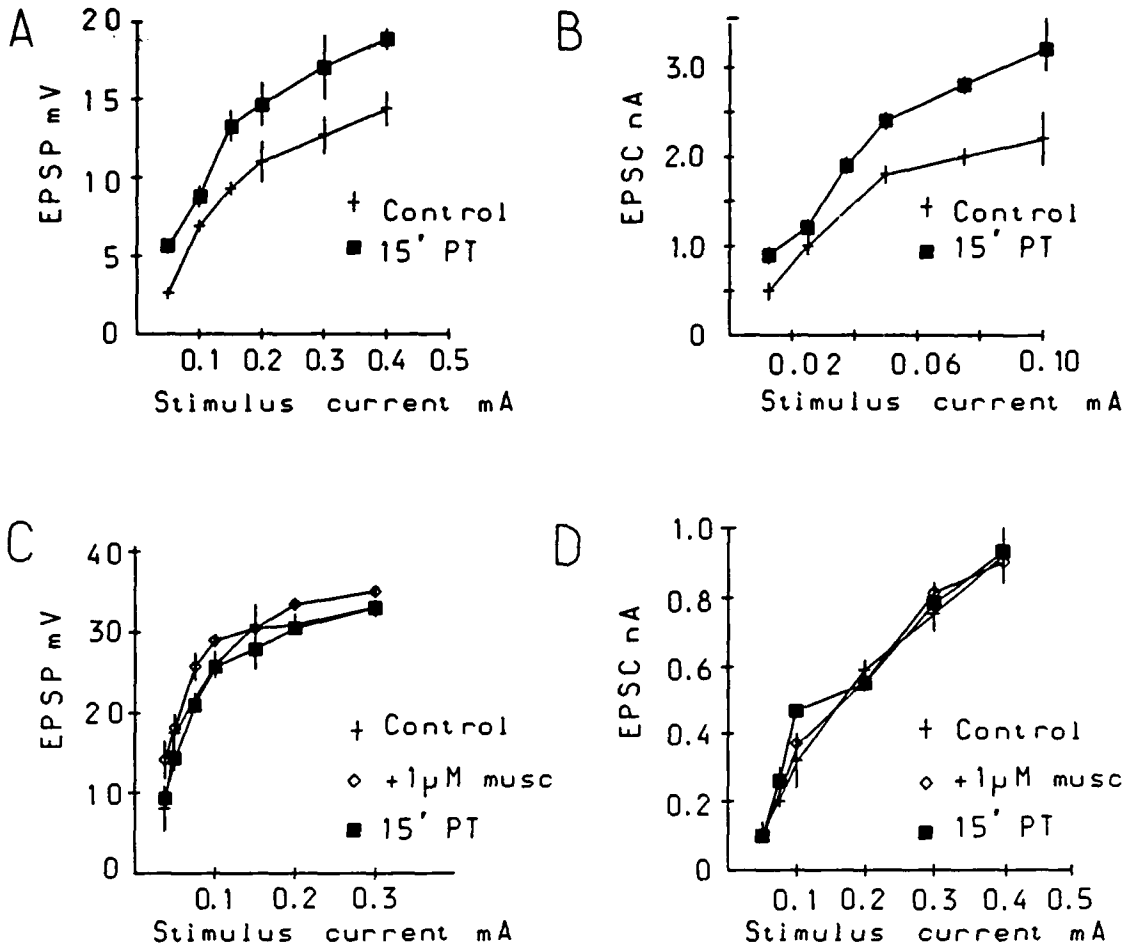

Fig. 2 Synaptic I–O relations measured under current and voltage clamp. (A) Control cell exhibiting LTP under current clamp. Peak EPSP amplitude is plotted versus stimulus current under control conditions and 15 min after tetanus. (B) I–O curves for a control cell (different cell) under voltage clamp, before and after tetanus. (C) Muscarine-treated cell under current clamp. Curves were constructed before and 15 min after superfusion of 1 μM muscarine and then 15 min after tetanus. In this cell there was a clear depression of the EPSP by muscarine, and no LTP was observed. (D) A similar experiment under voltage clamp (different cell). In this case 1 μM muscarine had little effect on the EPSC, and once again LTP was not obtained. (Points are mean of at least four determinations and error bars represent SEM).

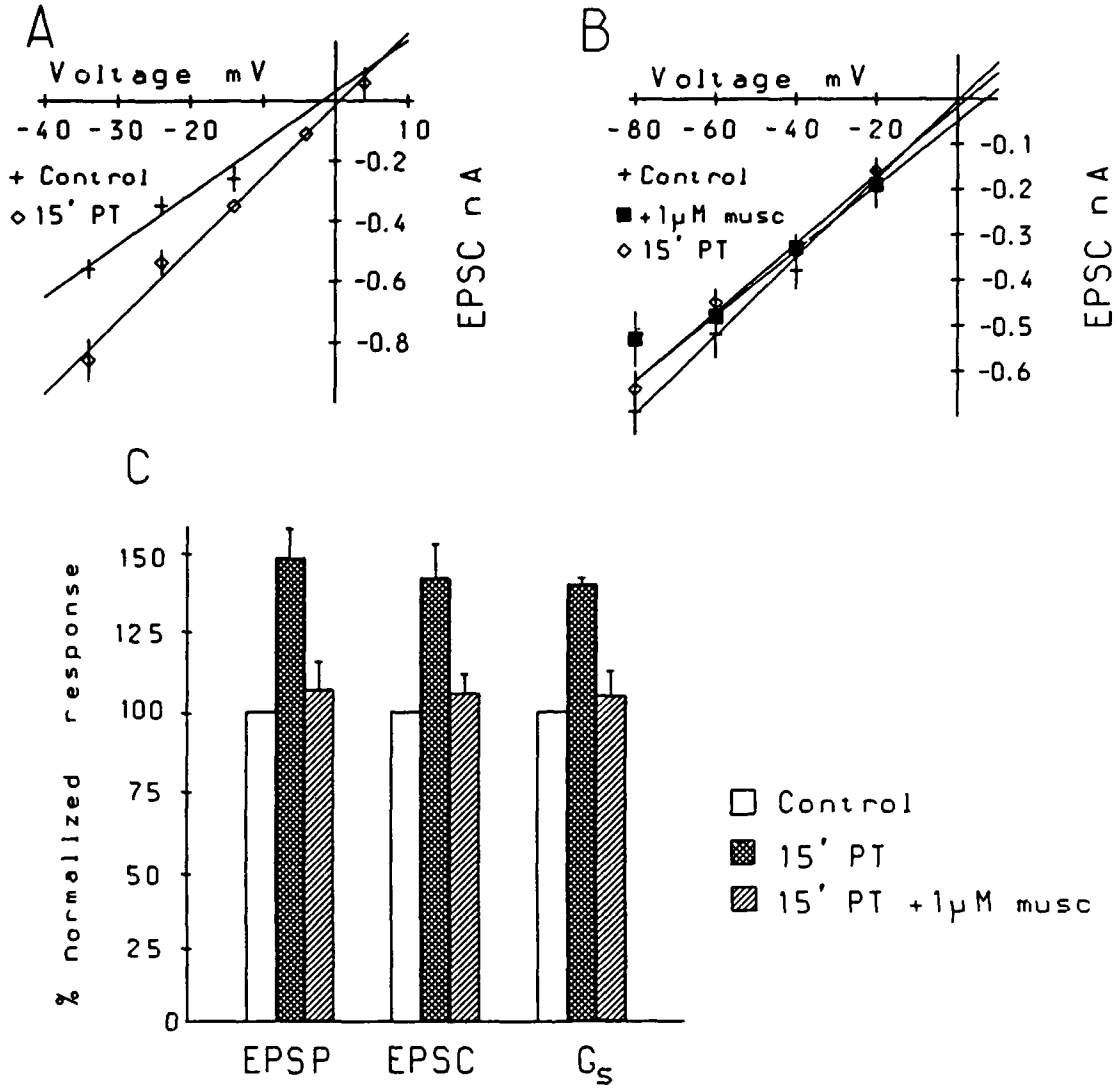

Fig. 3 Voltage-clamp analysis of mossy fiber synaptic conductance. (A) Current-voltage plot for a control cell, holding potential versus peak EPSC. The increase in slope of the line after tetanus (15′ PT) indicated an increase in g_s. (B) In a second cell treated with 1 μM muscarine g_s was slightly decreased, and LTP was blocked. Lines were determined by linear regression. (C) A summary of the action of 1 μM muscarine on LTP. Data normalized to pretetanus control (EPSP: 15′ PT, n=15; 1 μM n=10. EPSC: 15′ PT, n=11; 1 μM, n=7. g_s: 15′ PT, n=4; 1 μM, n=5).

Using cell-attached patch recordings, we observed three types of Ca channels in these neurons. The three different types were distinguished on the basis of different single-channel conductances recorded with isotonic barium chloride in the patch pipette. We observed channel openings with slope conductances of approximately 8 pS, 14 pS, and 27 pS (3). We found that NE, isoproterenol, and cAMP increased the activity of at least the 14 pS channel. We found no evidence for any change in single-channel conductance. Enhanced activity of the channel could be due to an increase in the number of channels or in the probability of opening.

A number of issues remain to be explored. These include a better characterization of properties of the three putative types of Ca channels. For example, we need to characterize the voltage dependencies, inactivation, and distribution of the channels [*e.g.*, location on the cell (soma vs dendrites) or among different cell types (granule cell vs CA3)]. Another particularly important issue is to test the effects of β-adrenoceptor agonists on Ca channels recorded on CA3 neurons. All of our single channel studies were done on granule cells because that was the cell type most amenable to whole-cell voltage clamping (granule cells in general provide a better space clamp than pyramidal cells). We also hope to explore effects of muscarinic agonists on Ca channels in light of our preliminary studies with muscarine and LTP.

3.5 Isolated mossy fiber terminals

During the last two years of funding, we were involved in the development of a preparation of isolated mossy fiber terminals (MFTs) suitable for electrophysiological analysis. Our initial efforts were directed toward a synaptosomal preparation in which hippocampi were homogenized and MFTs isolated by differential centrifugation. Although these procedures proved to be suitable for biochemical studies (15), for a variety of reasons, the electrophysiological recording of Ca channels from these large synaptosomes was difficult. During the last year, we tried a different approach that is a modification of the acutely exposed neuron preparation. Guinea pig slices were incubated with proteolytic enzymes and then dissociated with fine-tipped glass pipettes. In intact slices, we found that several vital fluorescent dyes, which are known to be reasonably selective for living presynaptic nerve terminals (13), produce intense staining of the mossy fiber synapses. After dissociation, there are also many of these mossy fiber terminals with similarly intense fluorescence. Using a Timm stain of these putative MFTs, we tentatively showed that the terminals with intense fluorescence in the range of 3-5 μm in diameter also stained for zinc, a characteristic feature of mossy fiber synapses.

Using cell-attached patch recordings in which the pipette contains isotonic barium chloride, we measured the activity of single voltage-dependent Ca channels from these isolated synaptic terminals (Figs. 4 & 5). In recent experiments, we recorded openings of at least three different amplitudes (5).

3.6 Development of single neuron and multi-neuron computer models

During the three-year tenure of this grant application, we slowly but steadily progressed in our development of a set of computer programs that simulate the electrophysiological characteristics of single hippocampal pyramidal neurons. Our program development took place primarily during the summer months, when we hired computer science students from Rice University. Initially, work was done to develop a program called MUNCH that simulates the passive electrophysiological characteristics of single neurons. This program was later modified to incorporate voltage-dependent ionic conductances and synaptic inputs, both excitatory and inhibitory. This program is now called NEURON and is in a fairly complete and final stage of development. Using a compartmental approach, this model allows one to simulate the passive electrotonic characteristics of the entire dendritic tree of any neuron for which morphometric data are available. Moreover, this model

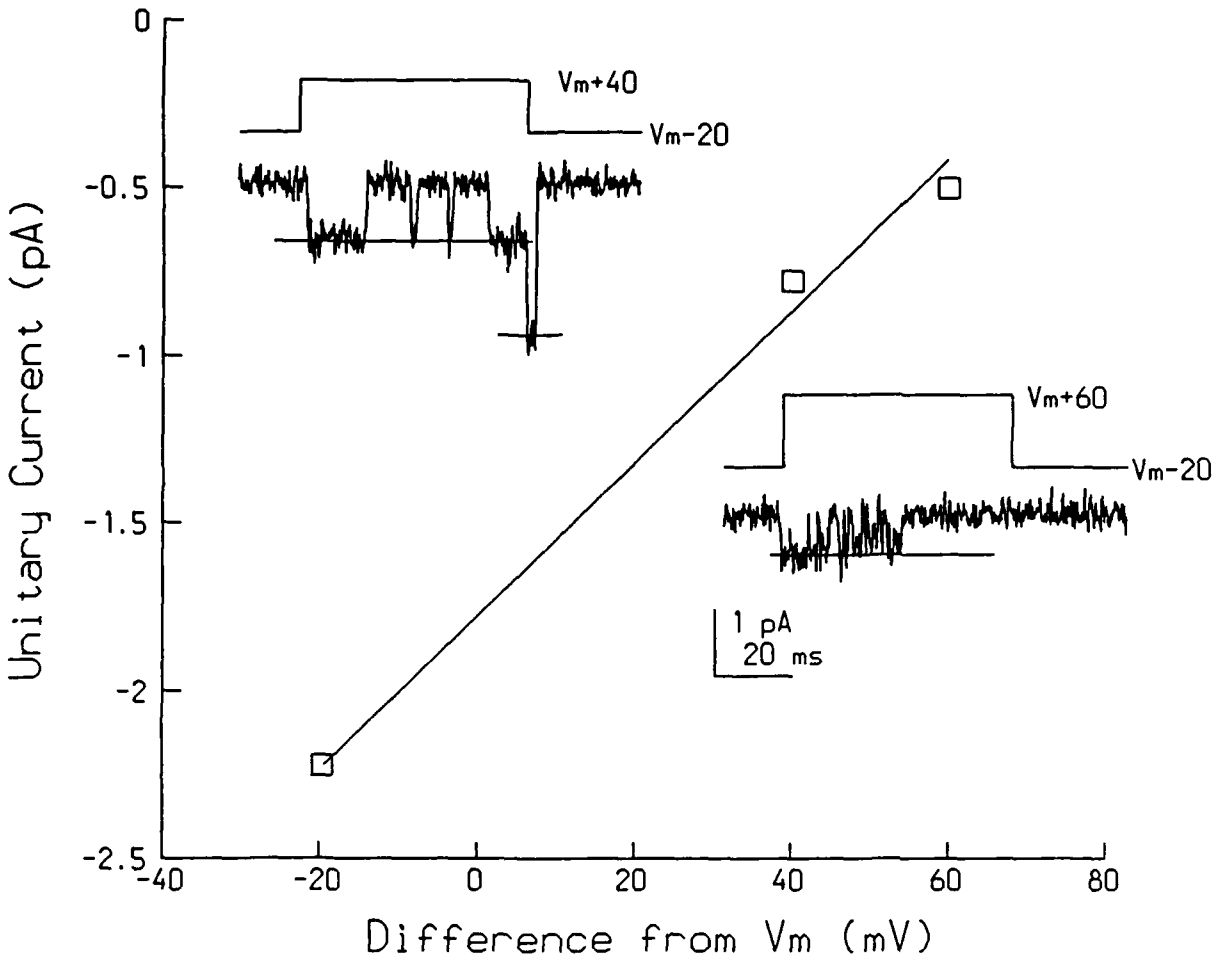

Fig. 4 Terminal-attached patch recordings of presynaptic CA channels from an isolated MFT. Patch pipette contained isotonic $BaCl_2$. Two step commands are shown as insets. Openings at three different voltage levels are shown, and the single channel currents for each of these are plotted on the graph. The slope conductance of this channel is 22 pS.

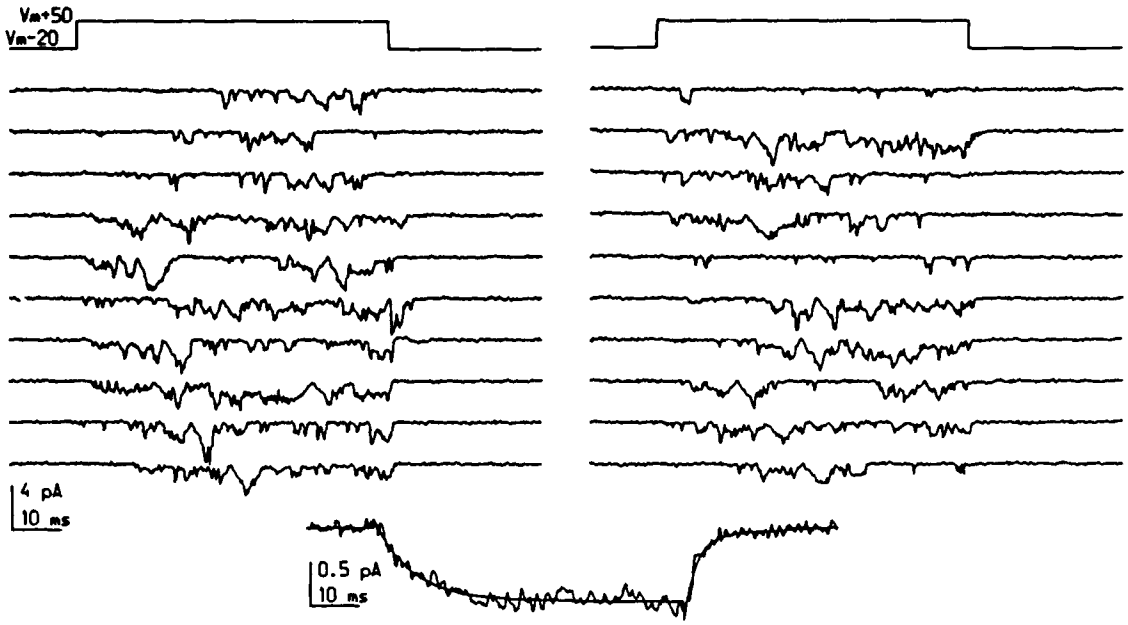

Fig. 5 Ensemble average of Ca channel currents recorded from an isolated MFT. Forty identical step commands (Vm -20 to Vm +50 mV) were given to a terminal-attached patch in which the pipette contained isotonic $BaCl_2$. The average of all the traces is shown at the bottom. The solid line represents the single exponential curve that best fits the data. We estimate that at least 17 channels were in the patch.

allows one to incorporate voltage-dependent sodium, potassium, and calcium conductances to any compartment of the model neuron. We have simulated neurons with up to 50 compartments, but in principle, there is no limit to the number of compartments. We can also add excitatory and inhibitory inputs with any desired conductances or kinetics. To make this model as realistic as possible, we can also incorporate current- or voltage-clamping with the model. This allows one to simulate not only the voltage response during current clamp experiments but also the measured current from a voltage clamp applied to the soma. This program is beginning to be used more extensively by people in the laboratory to help understand some of our experimental results; we believe it will continue to be of even more use in the future.

4 Publications

4.1 Full papers and review articles

1. Griffith, W.H., Brown, T.H., and Johnston, D. Voltage-clamp analysis of synaptic inhibition during long-term potentiation in hippocampus. *J. Neurophysiol.* 55:767–775, 1986.

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11. Johnston, D., Hopkins, W.F., and Gray, R. Norepinephrine enhances long-term potentiation at hippocampal mossy fiber synapses. In: *Synaptic Plasticity in the Hippocampus.* Haas, H.L. and Buzsàki, G., (eds.), Springer-Verlag: Berlin, 1988, pp. 57–60.

12. Hopkins, W.F. and Johnston, D. Noradrenergic modulation of synaptic plasticity in the hippocampus. In: *Developmental Neurophysiology.* Kellaway, P. and Purpura, D.P., (eds.), Johns Hopkins Univ. Press: Baltimore, (in press).

13. Johnston, D., Hopkins, W.F., and Gray, R. The role of norepinephrine in long-term potentiation at mossy fiber synapses in the hippocampus. In: *Neural Models of Plasticity.* Byrne, J.H. and Berry, W.O. (eds.), Academic Press, Inc.: San Diego, 1988, (in press).

14. Terrian, D.M., Johnston, D., Claiborne, B.J., Ansah-Yiadom, R., Strittmatter, W.J., and Rea, M.A. Glutamate and dynorphin release from a subcellular fraction enriched in hippocampal mossy fiber synaptosomes. *Brain Res. Bull.* (in press).

15. Williams, S.H. and Johnston, D. Muscarinic depression of an APV-insensitive form of LTP in hippocampal CA3 neurons. *Science* (in press). (Was submitted during the third year of funding and was accepted after the end of this grant.)

4.2 Abstracts

1. Gray, R. and Johnston, D. Macroscopic calcium currents in acutely-exposed neurons from adult hippocampal slices. *Biophys. J.* 47:66a, 1985.

2. Gray, R. and Johnston, D. Macroscopic calcium currents in acutely-exposed granule cells from adult hippocampus. *Soc. Neurosci. Abstr.* 11:792, 1985.

3. Gray, R. and Johnston, D. Multiple types of calcium channels in acutely-exposed neurons from adult hippocampus. *Biophys. J.* 49:432a, 1986.

4. Hopkins, W.F. and Johnston, D. Noradrenergic enhancement of long-term potentiation in disinhibited hippocampal slices. *Soc. Neurosci. Abstr.* 12:508, 1986.

5. Gray, R. and Johnston, D. Multiple types of calcium channels in acutely exposed neurons from the adult guinea pig hippocampus. *J. Gen. Physiol.* 88:25a–26a, 1986.

6. Johnston, D., Lebeda, F.J., Barber, S.O., Carnevale, N.T., and Gray, R. Functional reconstruction of hippocampal neurons. *Fifth Annu. Conf. Biomed. Engrg.*, 1987.

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9. Johnston, D. and Williams, S.H. Muscarine depresses long-term potentiation in CA3 neurones of the rat hippocampus. *J. Physiol.* (in press)

10. Fisher, R.E., Gray, R., and Johnston, D. β-adrenoceptor modulation of calcium channels in acutely exposed CA3 pyramidal neurons of adult guinea pig hippocampus. *Soc. Neurosci. Abstr.* (in press)

11. Gray, R. and Johnston, D. Recordings of single calcium channels from presynaptic mossy fiber terminals in adult guinea pig hippocampus. *Soc. Neurosci. Abstr.* (in press)

12. Jaffe, D.B. and Johnston, D. Depression of synaptic transmission by ω-conotoxin in the rat hippocampal slice. *Soc. Neurosci. Abstr.* (in press)

13. Williams, S.H. and Johnston, D. Muscarine depresses an APV-insensitive form of LTP in CA3 hippocampal neurons. *Soc. Neurosci. Abstr.* (in press)

5 Professional Personnel Associated With the Research Project

Daniel Johnston, Ph.D.—Principal Investigator
Frank J. Lebeda, Ph.D.—Investigator
Richard A. Gray, Ph.D.—Graduate Student; degree obtained during this grant
William F. Hopkins, Ph.D.—Graduate Student; degree obtained during this grant
Stephen Williams, Ph.D.—Research Associate
Stan Barber—Computer Systems Manager
Mahmud Haque—Computer Systems Manager
Judy Walker, M.S.—Research Technician
Pam Jones—Research Technician
Richmond Ansah-Yiadom—Research Technician
Ron Fisher—Graduate Student

6 Interactions

05/17/85	Society for Computer Simulation, University of Houston at Clear Lake, Clear Lake City, Texas. Presented lecture on neural modeling of single hippocampal neurons.
09/04/85	Conference on Excitatory Amino Acids and Epilepsy, France. Presented paper on the cellular basis of epilepsy.
10/85	Traveled to Air Force School of Aerospace Medicine, San Antonio, Texas, to visit and collaborate with Dr. David Terrian on project related to mossy fiber synaptosomes.
11/85	Dr. David Terrian from the US Air Force School of Aerospace Medicine, San Antonio, Texas, traveled to Houston to collaborate on a project related to mossy fiber synaptosomes.
11/85	Neuroscience Society Annual Meeting, Dallas, Texas. Rick Gray and Dan Johnston presented paper on noradrenergic enhancement of calcium current in hippocampal neurons.
11/12/85	Fall Task Review, Wright-Patterson Air Force Base, Dayton, Ohio. Presented talk on noradrenergic modulation of LTP.
11/25/85	Rice University Math Science Department, Rice University, Houston, Texas. Presented lecture on neural modeling and networks of hippocampal neurons.
01/06/86	McGill University, Department of Neuroscience, Montreal, Quebec. Presented lecture on cellular mechanisms of epileptogenesis.

01/86	Winter Conference on Brain Research, Keystone, Colorado. Discussed our work on mechanisms of LTP.
01/86	Dr. David Terrian from the US Air Force School of Aerospace Medicine, San Antonio, Texas, traveled to Houston to collaborate on a project related to mossy fiber synaptosomes.
02/86	Biophysical Society Meeting, San Francisco, California. Rick Gray and Dan Johnston presented paper on multiple types of calcium channels in hippocampal neurons.
03/31/86	Department of Pharmacology, Texas A&M University, College Station, Texas. Presented lecture on noradrenergic effects in hippocampus.
03/86	Traveled to Air Force School of Aerospace Medicine, San Antonio, Texas, to visit and collaborate with Dr. David Terrian on project related to mossy fiber synaptosomes.
04/04/86	Gave lecture at the University of Texas Health Science Center in Dallas.
04/6-10/86	Stan Barber to Masscomp Users' Society meeting in Boston.
04/23-24/86	Gave lecture ("Noradrenergic modulation of long-term synaptic potentiation in hippocampus") in Irvine, CA.
05/12-16/86	Attended Masscomp training course.
06/11-13/86	Attended Neurobehavioral Research Review Subcommittee Meeting in Washington, DC.
06/18/86	Judy Walker and Richmond Ansah-Yiadom visited Dr. Terrian's laboratory in San Antonio.
06/19-20/86	Dr. Stephen Smith, Dept. of Molecular and Neurobiology, Howard Hughes Institute & Yale Univ. Med. School. Visited, presented lecture on "Transformation of growth cone motility and structure by intracellular calcium and cyclic AMP."
06/26/86	Dr. Terrian visited the lab.
08/18-19/86	To Baltimore—spoke at ASPET-SOT.
09/3-7/86	Rick Gray presented poster at the Society of General Physiologists meeting, Woods Hole, Massachusetts.
09/10/86	Dr. Johnston and Richard Gray visited Dr. Terrian's laboratory in San Antonio.
09/22-23/86	Attended NIDA Technical Review Meeting on Neural Adaptation in Response to Intrinsic and Extrinsic Factors: Role in Drug Abuse, in Rockville, Maryland.
10/03/86	Attended Second Annual Symposium on Networks in Brain and Computer Architecture at North Texas State University in Denton.
10/22-25/86	Attended Neurobehavioral Research Review Committee in Washington, DC.
09/9-13/86	Dr. Johnston, Stephen Williams, and William Hopkins (Nov 9- 14) attended the Society for Neuroscience meeting in Washington, DC

02/11-13/87	Attended Neurobehavioral Research Review Committee meeting in Washington, DC.
02/18-19/87	Richmond Ansah-Yiadom to San Antonio to visit Dr. Terrian's laboratory.
02/23-24/87	Attended Biophysical Society meeting in New Orleans.
02/27/87	Drs. David Terrian and Michael Rea visited the laboratory.
03/12-13/87	Gave lecture (Functional reconstruction of hippocampal neurons) at Biomedical Engineering Research Conference in Houston.
03/27/87	Gave lecture (Cellular mechanisms of epilepsy) to MSTP students at Baylor.
03/30-31/87	Dr. David Terrian visited the laboratory.
04/26-05/1/87	Stan Barber to Masscomp Users' Society meeting, Boston.
04/28-05/01/87	Speaker at meeting (Neural Models of Plasticity: Theoretical and Empirical Approaches) at Woods Hole, Massachusetts.
06/10-13/87	NIMH Study Section, Washington, DC.
07/07-09/87	NIDA Study Section.
08/11-25/87	Budapest–IBRO Conference. Gave two presentations.
09/24-25/87	External Advisory Committee, Yale University.
10/06-09/87	NIMH Study Section, Washington, DC.
11/16-21/87	Society for Neuroscience meeting, New Orleans.
11/29-12/02/87	To San Antonio–Air Force Neuroscience Review.
02/2-4/88	Presented three lectures at the University of Pittsburgh, Physiology and Behavioral Neuroscience Departments.
02/10-13/88	NIMH Study Section, Washington, DC.

7 New Discoveries, Inventions, or Patent Applications

None.

8 References

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